(FILE 'HOME' ENTERED AT 10:27:39 ON 19 JUL 2002)

FILE 'CAPLUS, BIOSIS, CANCERLIT, MEDLINE, SCISEARCH, LIFESCI, EMBASE' ENTERED AT 10:38:53 ON 19 JUL 2002

```
L1             0 S MARTIPASE (A) INHIBITOR
L2             0 S MARTIPASE
L3             0 S MATRIPASE (A) INHIBITOR
L4             0 S MATRIPASE
L5            98 S MATRIPTASE
L6            40 DUPLICATE REMOVE L5 (58 DUPLICATES REMOVED)
L7             5 S MATRIPTASE (A) INHIBITOR
L8             5 DUPLICATE REMOVE L7 (0 DUPLICATES REMOVED)
L9             0 S MTS-P1 AND MPTSP1
L10            0 S MPTSP1
L11            0 S MPS-P1
L12            0 S MTS-P1
```

FILE 'USPATFULL, EUROPATFULL, JAPIO, PATOSWO' ENTERED AT 10:51:26 ON 19 JUL 2002

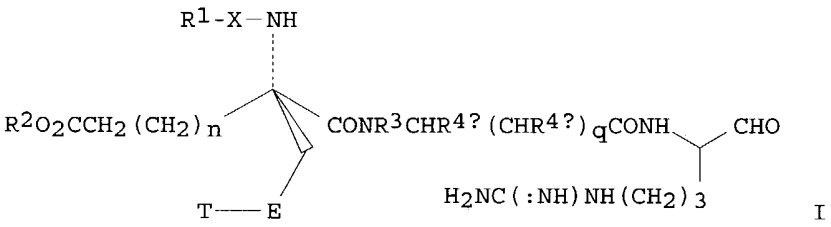
```
L13            5 S L5

=>
```

L8 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2002 ACS
AN 2002:185072 CAPLUS
DN 136:232549
TI Preparation of peptides as inhibitors of serine protease activity of matriptase or MTSP1
IN Duncan, David F.; Madison, Edwin L.; Semple, Joseph Edward; Coombs, Gary Samuel; Reiner, John Eugene; Ong, Edgar O.; Araldi, Gian Luca
PA Corvas International, Inc., USA
SO PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07C311-00
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 7, 63
FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002020475	A2	20020314	WO 2001-US28137	20010907

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2000-657986 A 20000908
OS MARPAT 136:232549
GI



I

AB The invention provides compds. I [X = CO, CO2, CONH, SO2, SO2NH or a direct link; R1 = (un)substituted alkyl, cycloalkyl, aryl, heterocycloalkyl, H when X is CONH, SO2, SO2NH or a direct link, etc.; R2 = H, alkyl; n = 0-3; R3 = H, Me; R4a, R4b = H, alkyl; q = 0-2; when q = 0, R3 and R4a form prolyl or prolyl derivs., pipecolyl, or azetidine-2-carbonyl groups which are in the S-configuration; E is a 5- or 6-membered arom. ring having 0-2 ring heteroatoms; T is H, OH, CH2OH, alkyl, cyano, an amidino, guanidino, amino or carbamoyl deriv.] which inhibit serine protease activity of matriptase or MTSP1. Also provided are pharmaceutical compns. for treating conditions ameliorated by inhibition of matriptase or MTSP1. Thus, (R)-5-[3-(diaminomethyl)phenyl]-4-[(1-formyl-(S)-4-guanidinobutylcarbamoylmethyl)carbamoyl]-4-(methoxycarbonylamino)pentanoic acid tert-Bu ester was prepd. and showed

IC50 < 100 nM for inhibition of matriptase activity.

ST peptide prepn **inhibitor matriptase** MTSP1

IT Peptides, preparation
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of peptides as inhibitors of serine protease activity of matriptase or MTSP1)

IT 9001-90-5, Plasmin 9002-04-4, Thrombin 9002-05-5, Factor xa 9002-07-7, Trypsin 37259-58-8, Serine protease 241475-96-7, Matriptase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prepn. of peptides as inhibitors of serine protease activity of matriptase or MTSP1)

IT 173656-55-8P 180312-24-7P 180312-25-8P 243969-94-0P 403669-10-3P
403669-11-4P 403669-12-5P 403669-13-6P 403669-14-7P 403669-15-8P
403669-16-9P 403669-17-0P 403669-18-1P 403669-19-2P 403669-20-5P
403669-21-6P 403669-22-7P 403669-23-8P 403669-24-9P 403669-25-0P
403669-26-1P 403669-27-2P 403669-28-3P 403669-29-4P 403669-30-7P
403669-31-8P 403669-32-9P 403669-33-0P 403669-34-1P 403669-35-2P
403669-36-3P 403669-37-4P 403669-38-5P 403669-39-6P 403669-40-9P
403669-41-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of peptides as inhibitors of serine protease activity of matriptase or MTSP1)

IT 79-22-1, Methyl chloroformate 630-19-3, Pivalaldehyde 2258-42-6, Acetic formic anhydride 2462-31-9 2605-67-6, Methoxycarbonylmethylenetriphenylphosphorane 28188-41-2, .alpha.-Bromo-m-tolunitrile 35000-38-5, tert-Butoxycarbonylmethylenetriphenylphosphorane 60022-62-0 193278-18-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of peptides as inhibitors of serine protease activity of matriptase or MTSP1)

IT 131148-70-4P 403669-00-1P 403669-01-2P 403669-02-3P 403669-03-4P
403669-04-5P 403669-05-6P 403669-06-7P 403669-07-8P 403669-08-9P
403669-09-0P 403669-42-1P 403669-43-2P 403669-44-3P 403669-45-4P
403669-46-5P 403669-47-6P 403669-48-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of peptides as inhibitors of serine protease activity of matriptase or MTSP1)

L8 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2002 ACS
AN 2001:935392 CAPLUS
DN 136:64107
TI Structure-based discovery of inhibitors of matriptase for the treatment of cancer and other conditions, and diagnostic methods
IN Lin, Chen-Yong; Dickson, Robert B.; Wang, Shaomeng; Enyedy, Istvan; Lee, Sheau-Ling
PA Georgetown University, USA
SO PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-00
CC 1-6 (Pharmacology)
Section cross-reference(s): 9

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001097794	A2	20011227	WO 2001-US18773	20010612

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 2000-213073P P 20000621

OS MARPAT 136:64107

AB A method is provided for inhibiting carcinoma progression in which matriptase plays a role in a subject in need of such inhibition. The method includes administering to a subject an effective amt. of a compd. comprising two pos. charged groups, which are the same or different. The groups are linked by a chem. group having a length of 5-30 A, and preferably 15-24 A. Diagnostic methods based on matriptase action and therapeutic methods involving inhibition of matriptase activity are provided.

ST **matriptase inhibitor** cancer treatment; cancer diagnosis matriptase; carcinoma treatment **matriptase inhibitor**

IT Esophagus
(Barrett's syndrome; matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)

IT Skin, neoplasm
(Bowen's disease, and Bowenoid papulosis; matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)

IT Keratosis
(actinic; matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)

IT Antitumor agents
(brain; matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)

IT Diagnosis
(cancer; matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)

IT Antitumor agents
(carcinoma; matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)

IT Uterus, disease
(cervix, dysplasia; matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)

IT Antitumor agents
(chronic myelocytic leukemia; matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)

IT Intestine, neoplasm
(colon, inhibitors; matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)

IT Antitumor agents
(colon; matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)

IT Neoplasm
(diagnosis; matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)

IT Mammary gland

(disease, pre-malignant condition; matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)
IT Uterus, neoplasm
(endometrium, inhibitors; matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)
IT Antitumor agents
(endometrium; matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)
IT Disease, animal
(erythroplasia of Queyrat; matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)
IT Antitumor agents
(head; matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)
IT Mammary gland
(hyperplasia, atypical ductal; matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)
IT Brain, neoplasm
Kidney, neoplasm
Ovary, neoplasm
Pancreas, neoplasm
Stomach, neoplasm
(inhibitors; matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)
IT Drug delivery systems
(injections, i.m.; matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)
IT Drug delivery systems
(injections, i.p.; matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)
IT Drug delivery systems
(injections, i.v.; matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)
IT Drug delivery systems
(injections; matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)
IT Drug delivery systems
(intratumoral; matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)
IT Antitumor agents
(kidney; matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)
IT Mouth
(leukoplakia; matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)
IT Antitumor agents
(mammary gland; matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)
IT Apoptosis
Drug delivery systems
Drug screening
Enzyme kinetics
Epithelium
Fluorescent substances
Imaging agents
Molecular modeling
Radioactive substances
Radiotherapy

(matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)

IT Hepatocyte growth factor
Zymogens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)

IT Antibodies
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)

IT Protein degradation
(matriptase substrate; matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)

IT Antibodies
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(monoclonal; matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)

IT Drug delivery systems
(nasal; matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)

IT Antitumor agents
(neck; matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)

IT Head
Mammary gland
Neck, anatomical
Prostate gland
(neoplasm, inhibitors; matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)

IT Drug delivery systems
(ophthalmic; matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)

IT Drug delivery systems
(oral; matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)

IT Antitumor agents
(ovary; matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)

IT Antitumor agents
(pancreas; matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)

IT Intestine, neoplasm
(polyp, adenomatous colorectal polyp; matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)

IT Antitumor agents
(prostate gland; matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)

IT Drug delivery systems
(rectal; matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)

IT Antitumor agents
(stomach; matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)

IT Drug delivery systems
(transdermal; matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)

IT Intestine, disease
(ulcerative colitis; matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)

IT Reproductive organ
(vulva, vulvar intraepithelial neoplasia; matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)
IT 9001-92-7, Protease
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(carcinoma progression-related protease cascade; matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)
IT 9002-04-4, Thrombin 9002-07-7, Trypsin 9039-53-6, Urokinase plasminogen activator 65147-09-3 73207-91-7 73617-90-0 82657-92-9,
Pro-urokinase plasminogen activator 88467-45-2 94367-21-2 109358-46-5 113866-20-9 241475-96-7, Matriptase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)
IT 10043-66-0, Iodine-131, biological studies 10098-91-6, Yttrium-90, biological studies 14133-76-7, Technetium-99, biological studies 14276-53-0, Copper-62, biological studies 14378-26-8, Rhenium-188, biological studies 14998-63-1, Rhenium-186, biological studies 15715-08-9, Iodine-123, biological studies 15750-15-9, Indium-111, biological studies
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)
IT 100-33-4 100-33-4D, analogs 101-62-2 101-62-2D, analogs 496-00-4 496-00-4D, analogs 3811-75-4 3811-75-4D, analogs 53230-08-3 53230-08-3D, analogs 57695-01-9 57695-01-9D, analogs 382595-04-2 382595-05-3 382595-06-4 382595-06-4D, analogs
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(matriptase inhibitors for treatment of cancer and other conditions, and diagnostic methods)

L8 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2002 ACS
AN 2001:651017 CAPLUS
DN 136:54018
TI Synthesis and evaluation of the sunflower derived trypsin inhibitor as a potent inhibitor of the type II transmembrane serine protease, matriptase
AU Long, Y.-Q.; Lee, S.-L.; Lin, C.-Y.; Enyedy, I. J.; Wang, S.; Li, P.; Dickson, R. B.; Roller, P. P.
CS Laboratory of Medicinal Chemistry, FCRDC, National Cancer Institute, NIH, Frederick, MD, 21702, USA
SO Bioorganic & Medicinal Chemistry Letters (2001), 11(18), 2515-2519
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
CC 34-4 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 6, 7, 9, 11, 22
AB We report here the synthesis of a 14-amino acid long bicyclic peptide, previously isolated from sunflower seeds. This peptide, termed sunflower trypsin inhibitor (SFTI-1), is one of the most potent naturally occurring small-mol. trypsin inhibitors. In addn. to inhibiting trypsin, the synthetic SFTI-1 is also a very potent inhibitor, with a Ki of 0.92 nM, of
the recently identified epithelial serine protease, termed 'matriptase'.
ST trypsin inhibitor peptide bicyclic sunflower deriv solid phase synthesis; peptide bicyclic sunflower deriv prepn **matriptase inhibitor** conformation; SFTI1 prepn mol dynamics simulation secondary structure Xray

IT Conformation
(conformation and secondary structure by X-ray of sunflower trypsin inhibitor)
IT Simulation and Modeling, physicochemical
(mol. dynamics; secondary structure and conformation of sunflower trypsin inhibitor by mol. dynamics simulation and modeling)
IT Natural products
RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and evaluation of sunflower derived bicyclic peptide trypsin selective inhibitor as inhibitor of type II transmembrane serine protease matriptase)
IT Secondary structure
(secondary structure and conformation of sunflower trypsin inhibitor by mol. dynamics simulation and modeling)
IT Sunflower
(seed; prepn. and evaluation of sunflower derived bicyclic peptide trypsin selective inhibitor as inhibitor of type II transmembrane serine protease matriptase)
IT Solid phase synthesis
(solid phase synthesis and evaluation of sunflower derived bicyclic peptide trypsin selective inhibitor as inhibitor of type II transmembrane serine protease matriptase)
IT Proteins
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(solid phase synthesis and evaluation of sunflower derived bicyclic peptide trypsin selective inhibitor as inhibitor of type II transmembrane serine protease matriptase)
IT Peptides, preparation
RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(solid phase synthesis and evaluation of sunflower derived bicyclic peptide trypsin selective inhibitor as inhibitor of type II transmembrane serine protease matriptase)
IT Seed
(sunflower; prepn. and evaluation of sunflower derived bicyclic peptide trypsin selective inhibitor as inhibitor of type II transmembrane serine protease matriptase)
IT 9002-04-4, Thrombin 9002-07-7, Trypsin 9039-53-6, Urokinase-type plasminogen activator 37330-34-0, Bowman-Birk inhibitor 65147-09-3 109358-46-5 113866-20-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prepn. and evaluation of sunflower derived bicyclic peptide trypsin selective inhibitor as inhibitor of type II transmembrane serine protease matriptase)
IT 241475-96-7, Matriptase
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(prepn. and evaluation of sunflower derived bicyclic peptide trypsin selective inhibitor as inhibitor of type II transmembrane serine protease matriptase)
IT 245080-24-4P, SFTI-1
RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(prepn. and evaluation of sunflower derived bicyclic peptide trypsin selective inhibitor as inhibitor of type II transmembrane serine protease matriptase)

RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Altschul, S; Nucleic Acids Res 1997, V25, P3389 CAPLUS
(2) Andricioaei, I; Physical Rev E 1996, V53, PR3055 CAPLUS
(3) Berman, H; Nucleic Acids Res 2000, V28, P235 CAPLUS
(4) Bernstein, F; J Mol Biol 1977, V112, P535 CAPLUS
(5) Brooks, B; J Comput Chem 1983, V4, P187 CAPLUS
(6) Enyedy, I; J Med Chem 2001, V44, P1349 CAPLUS
(7) Hooper, J; J Biol Chem 2001, V276, P857 CAPLUS
(8) Kasher, R; J Mol Biol 1999, V292, P421 CAPLUS
(9) Kawaguchi, T; J Biol Chem 1997, V272, P27558 CAPLUS
(10) Kim, M; Immunogenetics 1999, V49, P420 CAPLUS
(11) Laskowski, M; Annu Rev Biochem 1980, V49, P593 CAPLUS
(12) Lee, S; J Biol Chem 2000, V275, P36720 CAPLUS
(13) Li, Y; J Biochem 1994, V116, P18 CAPLUS
(14) Lin, C; J Biol Chem 1997, V272, P9147 CAPLUS
(15) Lin, C; J Biol Chem 1999, V274, P18231 CAPLUS
(16) Lin, C; J Biol Chem 1999, V274, P18237 CAPLUS
(17) Luckett, S; J Mol Biol 1999, V290, P525 CAPLUS
(18) Pak, Y; J Phys Chem B 2000, V104, P354 CAPLUS
(19) Rydel, T; J Mol Biol 1991, V221, P583 CAPLUS
(20) Sali, A; Proteins: Struct Funct Genet 1995, V23, P318 CAPLUS
(21) Shewry, P; Advan Botan Res 1997, V26, P135 CAPLUS
(22) Takeuchi, T; J Biol Chem 2000, V275, P26333 CAPLUS
(23) Wenzel, H; Peptides: Synthesis, Structure and Applications 1995, P321 CAPLUS

L8 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2002 ACS
AN 2001:221298 CAPLUS
DN 135:162
TI Structure-based approach for the discovery of bis-benzamidines as novel inhibitors of matriptase
AU Enyedy, Istvan J.; Lee, Sheau-Ling; Kuo, Angera H.; Dickson, Robert B.; Lin, Chen-Yong; Wang, Shaomeng
CS Structural Biology and Cancer Drug Discovery Program Department of Oncology, Lombardi Cancer Center Georgetown University Medical Center, Washington, DC, 20007, USA
SO Journal of Medicinal Chemistry (2001), 44(9), 1349-1355
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
CC 1-3 (Pharmacology)
Section cross-reference(s): 7
AB Matriptase, a trypsin-like serine protease, which may be involved in tissue remodeling, cancer invasion, and metastasis. Potent and selective matriptase inhibitors not only would be useful pharmacol. tools for further elucidation of the role of matriptase in these processes but also could have therapeutic potential for the treatment and/or prevention of cancers. We report herein the structure-based approach for the discovery of bis-benzamidines as a novel class of potent matriptase inhibitors. The lead compd., hexamidine (1), inhibits not only the proteolytic activity of matriptase, (Ki = 924 nM) but also of thrombin (Ki = 224 nM). By testing several available analogs, we identified a new analog (7) that has a Ki = 208 nM against matriptase and has only weak inhibitory activity against

thrombin (Ki = 2670 nM), thus displaying a 13-fold selectivity toward matriptase. Our results demonstrated that structure-based database screening is effective in the discovery of matriptase inhibitors and that bis-benzamidines represent a class of promising matriptase inhibitors that can be used for further drug design studies. Finally, our study suggested that there is sufficient structural differences between matriptase and its closely related serine proteases, such as thrombin, for the design of potent and selective matriptase inhibitors.

ST bisbenzamidine structure **matriptase inhibitor** design screening; antimetastatic benzamidine **matriptase inhibitor** SAR thrombin; database screening benzamidine antitumor **matriptase inhibitor**; protein sequence **matriptase inhibitor** structure design

IT Structure-activity relationship
(antimetastatic; structure-based approach for bis-benzamidines discovery as novel matriptase inhibitors)

IT Structure-activity relationship
(antitumor; structure-based approach for bis-benzamidines discovery as novel matriptase inhibitors)

IT Structure-activity relationship
(enzyme-inhibiting, matriptase; structure-based approach for bis-benzamidines discovery as novel matriptase inhibitors)

IT Conformation
Databases
Drug design
Molecular modeling
Protein sequences
(structure-based approach for bis-benzamidines discovery as novel matriptase inhibitors)

IT Drug screening
(structure-based database; structure-based approach for bis-benzamidines discovery as novel matriptase inhibitors)

IT 241143-23-7, Matriptase (human clone SNC19 precursor)
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(amino acid sequence; structure-based approach for bis-benzamidines discovery as novel matriptase inhibitors)

IT 100-33-4 496-00-4 3811-75-4, Hexamidine 35872-68-5 53230-08-3 80498-64-2 340809-91-8
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(structure-based approach for bis-benzamidines discovery as novel matriptase inhibitors)

IT 3256-24-4 9002-04-4, Thrombin 227171-07-5, Gen Bank AF118224 241475-96-7, Matriptase
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(structure-based approach for bis-benzamidines discovery as novel matriptase inhibitors)

RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Altschul, S; Nucleic Acids Res 1997, V25, P3389 CAPLUS
(2) Babine, R; Chem Rev 1997, V97, P1359 CAPLUS
(3) Bemis, G; J Comput-Aid Mol Des 1992, V6, P607 MEDLINE
(4) Benaud, C; Breast Cancer Res Treat 1998, V50, P97 CAPLUS

(5) Bernstein, F; J Mol Biol 1977, V112, P535 CAPLUS
(6) Brooks, B; J Comput Chem 1983, V4, P187 CAPLUS
(7) Brunger, A; Proteins:Struct Funct Genet 1988, V4, P148 CAPLUS
(8) Durell, S; J Phys Chem 1994, V98, P2198 CAPLUS
(9) Fersht, A; Structure and Mechanism in Protein Science A Guide to Enzyme Catalysis and Protein Folding 1999, P1
(10) Jonassen, I; J Mol Biol 2000, V304, P599 CAPLUS
(11) Knegtel, R; J Mol Biol 1997, V266, P424 CAPLUS
(12) Lee, S; J Biol Chem 2000, V275, P36720 CAPLUS
(13) Leung, D; J Med Chem 2000, V43, P305 CAPLUS
(14) Lin, C; J Biol Chem 1997, V272, P9147 CAPLUS
(15) Lin, C; J Biol Chem 1999, V274, P18231 CAPLUS
(16) Lin, C; J Biol Chem 1999, V274, P18237 CAPLUS
(17) Makino, S; J Comput Chem 1997, V18, P1812 CAPLUS
(18) Mignatti, P; Physiol Rev 1993, V73, P161 CAPLUS
(19) Milne, G; J Chem Inf Comput Sci 1994, V34, P1219 CAPLUS
(20) Momany, F; J Comput Chem 1992, V13, P888 CAPLUS
(21) Oberst, M; J Women's Cancer, in press 2001
(22) Pak, Y; J Phys Chem B 2000, V104, P354 CAPLUS
(23) Robinson, R; J Med Chem 2000, V43, P2293 CAPLUS
(24) Sali, A; Curr Opin Biotechnol 1995, V6, P437 CAPLUS
(25) Sali, A; Proteins:Struct Funct Genet 1995, V23, P318 CAPLUS
(26) Takeuchi, T; J Biol Chem 2000, V275, P26333 CAPLUS
(27) Takeuchi, T; Proc Natl Acad Sci U S A 1999, V96, P11054 CAPLUS
(28) Weber, P; Biochemistry 1995, V34, P3750 CAPLUS
(29) Westermarck, J; FASEB J 1999, V13, P781 CAPLUS

L8 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2002 ACS
AN 2000:645893 CAPLUS
DN 133:234748
TI Matriptase, a serine protease and its applications in detection of breast or other cancers
IN Dickson, Robert B.; Lin, Chen-Yong; Johnson, Michael; Wang, Shaomeng; Enyedy, Istvan
PA Georgetown University, USA
SO PCT Int. Appl., 116 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K049-00
CC 9-10 (Biochemical Methods)
Section cross-reference(s): 8, 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000053232	A1	20000914	WO 2000-US6111	20000310
	W: CA, JP, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	EP 1161266	A1	20011212	EP 2000-914875	20000310
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRAI	US 1999-124006P	P	19990312		
	WO 2000-US6111	W	20000310		

AB The invention is directed to a method of detecting a malignancy or a pre-malignant lesion in breast or other tissue, or a pathol. condition, by detecting the presence of single-chain or two-chain forms of matriptase in the tissue. The invention is further directed to a method of treating

malignancies, which have the phenotype of matriptase prodn. by administering a tumor formation inhibiting effective amt. of a conc. of Bowman-Birk inhibitor (BBIC), or other **matriptase inhibitor**. The invention also is directed to nucleic acids encoding a matriptase protein or fragments thereof, and their use for structure elucidation and modeling to identify other inhibitors of matriptase, as well as to methods of identifying matriptase modulating agents, including activators and inhibitors.

ST matriptase diagnosis breast cancer sequence; antitumor matriptase diagnosis cancer

IT Skin, neoplasm
(Bowen's disease; matriptase, a serine protease and its applications in detection of breast or other cancers)

IT Keratosis
(actinic; matriptase, a serine protease and its applications in detection of breast or other cancers)

IT Mammary gland
(atypical ductal hyperplasia; matriptase, a serine protease and its applications in detection of breast or other cancers)

IT Uterus
(cervix, dysplasia; matriptase, a serine protease and its applications in detection of breast or other cancers)

IT Esophagus
(disease, Barrett's epithelium; matriptase, a serine protease and its applications in detection of breast or other cancers)

IT Imaging
(fluorescent; matriptase, a serine protease and its applications in detection of breast or other cancers)

IT Immunoglobulins
RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(fragments; matriptase, a serine protease and its applications in detection of breast or other cancers)

IT Dimerization
(inhibition of; matriptase, a serine protease and its applications in detection of breast or other cancers)

IT Proteins, specific or class
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(labeled; matriptase, a serine protease and its applications in detection of breast or other cancers)

IT Mouth
(leukoplakia; matriptase, a serine protease and its applications in detection of breast or other cancers)

IT Antitumor agents
(matriptase inhibitors; matriptase, a serine protease and its applications in detection of breast or other cancers)

IT Animal tissue culture
Body fluid
Diagnosis
Epithelium
Fluorescent indicators
Genetic vectors
Imaging
Immunoassay
Molecular cloning
Protein sequences
Transformation, genetic

cDNA sequences
(matriptase, a serine protease and its applications in detection of breast or other cancers)

IT Antibodies
RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(matriptase-specific; matriptase, a serine protease and its applications in detection of breast or other cancers)

IT Antitumor agents
Neoplasm
(metastasis; matriptase, a serine protease and its applications in detection of breast or other cancers)

IT Antibodies
RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(monoclonal, matriptase-specific; matriptase, a serine protease and its applications in detection of breast or other cancers)

IT Mammary gland
(neoplasm; matriptase, a serine protease and its applications in detection of breast or other cancers)

IT Intestine, neoplasm
(polyp, adenomatous colorectal; matriptase, a serine protease and its applications in detection of breast or other cancers)

IT Protein motifs
(transmembrane domain; matriptase, a serine protease and its applications in detection of breast or other cancers)

IT Intestine, disease
(ulcerative colitis; matriptase, a serine protease and its applications in detection of breast or other cancers)

IT Reproductive organ
(vulva, neoplasm; matriptase, a serine protease and its applications in detection of breast or other cancers)

IT 241143-23-7, GenBank AF118224-derived protein GI 5359675 292886-21-6, Matriptase (human truncated isoform)
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(amino acid sequence; matriptase, a serine protease and its applications in detection of breast or other cancers)

IT 241475-96-7, Matriptase
RL: ANT (Analyte); BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(matriptase, a serine protease and its applications in detection of breast or other cancers)

IT 37330-34-0, Bowman-Birk **inhibitor**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**matriptase**, a serine protease and its applications in detection of breast or other cancers)

IT 227171-07-5, GenBank AF118224 292601-36-6

RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP
(Properties); BIOL (Biological study); OCCU (Occurrence)
(nucleotide sequence; matriptase, a serine protease and its applications in detection of breast or other cancers)
IT 10043-66-0, Iodine 131, biological studies 10098-91-6, Yttrium 90, biological studies 14133-76-7, Technetium 99, biological studies 14276-53-0, Copper 62, biological studies 14378-26-8, Rhenium 188, biological studies 14998-63-1, Rhenium 186, biological studies 15715-08-9, Iodine 123, biological studies 15750-15-9, Indium 111, biological studies
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(radiolabel; matriptase, a serine protease and its applications in detection of breast or other cancers)
IT 292888-12-1, 2: PN: WO0053232 PAGE: 53 unclaimed DNA 292888-13-2, 3: PN:
WO0053232 PAGE: 53 unclaimed DNA 292888-14-3, 4: PN: WO0053232 PAGE: 59 unclaimed DNA 292888-15-4, 5: PN: WO0053232 PAGE: 59 unclaimed DNA
RL: PRP (Properties)
(unclaimed nucleotide sequence; matriptase, a serine protease and its applications in detection of breast or other cancers)
IT 292888-16-5 292888-17-6 292888-18-7 292888-19-8 292888-20-1
292888-21-2 292888-22-3 292888-23-4 292888-24-5 292888-25-6
292888-26-7 292888-27-8 292888-28-9 292888-29-0 292888-30-3
292888-31-4 293307-69-4 293307-70-7 293307-71-8 293307-72-9
RL: PRP (Properties)
(unclaimed protein sequence; matriptase, a serine protease and its applications in detection of breast or other cancers)
IT 292820-68-9 292820-69-0 292820-70-3 292820-71-4
RL: PRP (Properties)
(unclaimed sequence; matriptase, a serine protease and its applications
in detection of breast or other cancers)
RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Blaney; US 5680331 A 1997 CAPLUS
(2) Kennedy; US 5505946 A 1996
(3) Kennedy; Cancer Research 1996, V56, P679 CAPLUS
(4) Kennedy, A; American Journal of Clinical Nutrition 1998, V68, P1406S CAPLUS
(5) Lin; Journal of Biological Chemistry 1997, V272(14), P9147 CAPLUS
(6) Lin; Journal of Biological Chemistry 1999, V274(26), P18231 CAPLUS
(7) Lin; Journal of Biological Chemistry 1999, V274(26), P18237 CAPLUS
(8) McKenzie; US 5084266 A 1992
(9) Yamamoto; Journal of Medicinal Chemistry 1998, V41(8), P1209 CAPLUS

=>

13 ANSWER 1 OF 5 USPATFULL
AN 2001:163328 USPATFULL
TI Transmembrane serine protease overexpressed in ovarian carcinoma and uses thereof
IN O'Brien, Timothy J., Little Rock, AR, United States
Underwood, Lowell J., Little Rock, AR, United States
PA The Board of Trustees of the University of Arkansas, Little Rock, AR, United States (U.S. corporation)
PI US 6294663 B1 20010925
AI US 2000-518046 20000302 (9)
RLI Continuation-in-part of Ser. No. US 1999-261416, filed on 3 Mar 1999
DT Utility
FS GRANTED
EXNAM Primary Examiner: Bansal, Geetha P.; Assistant Examiner: Canella, Karen A.
LREP Adle, Benjamin Aaron
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN 15 Drawing Figure(s); 12 Drawing Page(s)
LN.CNT 1538
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 2 OF 5 PATOSWO COPYRIGHT 2002 WILA
AN 2002:413602 PATOSWO ED 20020321 EW 200211 FS OS
TI INHIBITORS OF SERINE PROTEASE ACTIVITY OF **MATRIPTASE** OR MTSP1.
IN DUNCAN, David, F., 12550 Carmel Creek Road #107, San Diego, CA 92130, US;
MADISON, Edwin, L., 11005 Cedarcrest Way, San Diego, CA 92121, US;
SEMPLE, Joseph, Edward, 9711 Caminito Pudregal, San Diego, CA 92131, US;
COOMBS, Gary, Samuel, 8757 Libra Drive, San Diego, CA 92126, US;
REINER, John, Eugene, 7510 Charmant Drive #724, San Diego, CA 92122, US;
ONG, Edgar, O., 7270 Calle Cristobal # 56, San Diego, CA 92126, US;
ARALDI, Gian, Luca, 22 Hillview Lane, Plymouth, MA 02360, US
PA CORVAS INTERNATIONAL, INC., 3030 Science Park Drive, San Diego, CA 92121, US (except US);
DUNCAN, David, F., 12550 Carmel Creek Road #107, San Diego, CA 92130, US
(only US);
MADISON, Edwin, L., 11005 Cedarcrest Way, San Diego, CA 92121, US (only US);
SEMPLE, Joseph, Edward, 9711 Caminito Pudregal, San Diego, CA 92131, US (only US);
COOMBS, Gary, Samuel, 8757 Libra Drive, San Diego, CA 92126, US (only US);
REINER, John, Eugene, 7510 Charmant Drive #724, San Diego, CA 92122, US (only US);
ONG, Edgar, O., 7270 Calle Cristobal # 56, San Diego, CA 92126, US (only
US);
ARALDI, Gian, Luca, 22 Hillview Lane, Plymouth, MA 02360, US (only US
AG BIGGS, Suzanne, Pillsbury Winthrop LLP, 50 Fremont Street, San Francisco, CA 94105, US
SO Wila-IPA-2002-H11-T1
DT Patent
LA Application in English
DS W AE; W AG; W AL; W AM; W AT; W AU; W AZ; W BA; W BB; W BG; W BR; W BY; W BZ; W CA; W CH; W CN; W CO; W CR; W CU; W CZ; W DE; W DK; W DM; W DZ; W EC; W EE; W ES; W FI; W GB; W GD; W GE; W GH; W GM; W HR; W HU; W ID;

W IL; W IN; W IS; W JP; W KE; W KG; W KP; W KR; W KZ; W LC; W LK; W LR;
W LS; W LT; W LU; W LV; W MA; W MD; W MG; W MK; W MN; W MW; W MX; W MZ;
W NO; W NZ; W PH; W PL; W PT; W RO; W RU; W SD; W SE; W SG; W SI; W SK;
W SL; W TJ; W TM; W TR; W TT; W TZ; W UA; W UG; W US; W UZ; W VN; W YU;
W ZA; W ZW;
RW AT; RW BE; RW CH; RW CY; RW DE; RW DK; RW ES; RW FI; RW FR; RW GB;
RW
GR; RW IE; RW IT; RW LU; RW MC; RW NL; RW PT; RW SE; RW TR; RW AM; RW
AZ; RW BY; RW KG; RW KZ; RW MD; RW RU; RW TJ; RW TM; RW GH; RW GM; RW
KE; RW LS; RW MW; RW MZ; RW SD; RW SL; RW SZ; RW TZ; RW UG; RW ZW; RW
BF; RW BJ; RW CF; RW CG; RW CI; RW CM; RW GA; RW GN; RW GQ; RW GW; RW
ML; RW MR; RW NE; RW SN; RW TD; RW TG
PIT WOA2 PCT-PUBLICATION
PI WO 2002020475 A2 20020314
OD 20020314
AI WO 2001-US28137 20010907
PRAI US 2000-657986 20000908

L13 ANSWER 3 OF 5 PATOSWO COPYRIGHT 2002 WILA
AN 2002:144708 PATOSWO ED 20020207 EW 200205 FS OS
TI REGULATION OF HUMAN **MATRIPTASE**-LIKE SERINE PROTEASE.
IN XIAO, Yonghong, 78 Dana Street #1, Cambridge, MA 02138, US
PA BAYER AKTIENGESELLSCHAFT, 51368 Leverkusen, DE (except US);
XIAO, Yonghong, 78 Dana Street #1, Cambridge, MA 02138, US (only US
AG BAYER AKTIENGESELLSCHAFT, 51368 Leverkusen, DE
SO Wila-IPA-2002-H05-T1
DT Patent
LA Application in English
DS W AE; W AG; W AL; W AM; W AT; W AU; W AZ; W BA; W BB; W BG; W BR; W BY;
W BZ; W CA; W CH; W CN; W CO; W CR; W CU; W CZ; W DE; W DK; W DM; W DZ;
W EC; W EE; W ES; W FI; W GB; W GD; W GE; W GH; W GM; W HR; W HU; W ID;
W IL; W IN; W IS; W JP; W KE; W KG; W KP; W KR; W KZ; W LC; W LK; W LR;
W LS; W LT; W LU; W LV; W MA; W MD; W MG; W MK; W MN; W MW; W MX; W MZ;
W NO; W NZ; W PL; W PT; W RO; W RU; W SD; W SE; W SG; W SI; W SK; W SL;
W TJ; W TM; W TR; W TT; W TZ; W UA; W UG; W US; W UZ; W VN; W YU; W ZA;
W ZW;
RW AT; RW BE; RW CH; RW CY; RW DE; RW DK; RW ES; RW FI; RW FR; RW GB;
RW
GR; RW IE; RW IT; RW LU; RW MC; RW NL; RW PT; RW SE; RW TR; RW AM; RW
AZ; RW BY; RW KG; RW KZ; RW MD; RW RU; RW TJ; RW TM; RW GH; RW GM; RW
KE; RW LS; RW MW; RW MZ; RW SD; RW SL; RW SZ; RW TZ; RW UG; RW ZW; RW
BF; RW BJ; RW CF; RW CG; RW CI; RW CM; RW GA; RW GN; RW GW; RW ML; RW
MR; RW NE; RW SN; RW TD; RW TG
PIT WOA2 PCT-PUBLICATION
PI WO 2002008392 A2 20020131
OD 20020131
AI WO 2001-EP8182 20010716
PRAI US 2000-220807 20000725
US 2001-280109 20010402

L13 ANSWER 4 OF 5 PATOSWO COPYRIGHT 2002 WILA
AN 2001:1664499 PATOSWO ED 20020110 EW 200152 FS OS
TI STRUCTURE BASED DISCOVERY OF INHIBITORS OF **MATRIPTASE** FOR THE
TREATMENT OF CANCER AND OTHER CONDITIONS.
IN LIN, Chen-Yong, 7610 Shreve Road, Falls Church, VA 22043, US;
DICKSON, Robert, B., 9900 Hillridge Road, Kensington, MD 20845, US;
WANG, Shaomeng, 1112 Regal Oak Drive, Rockville, MD 20852, US;
ENYEDY, Istvan, Apt. 302, 3216 Chillum Road, Mount Ranier, MD 20712,
US;
LEE, Sheau-Ling, 7328 Parkwood Court, Falls Church, VA 22042, US

PA GEORGETOWN UNIVERSITY, 3900 Reservoir Road, N.W., Washington, DC 20007, US (except US);
LIN, Chen-Yong, 7610 Shreve Road, Falls Church, VA 22043, US (only US);
DICKSON, Robert, B., 9900 Hillridge Road, Kensington, MD 20845, US (only US);
WANG, Shaomeng, 1112 Regal Oak Drive, Rockville, MD 20852, US (only US);
ENYEDY, Istvan, Apt. 302, 3216 Chillum Road, Mount Ranier, MD 20712, US (only US);
LEE, Sheau-Ling, 7328 Parkwood Court, Falls Church, VA 22042, US (only US
AG TESKIN, Robin, L. et al., Pillsbury Winthrop LLP, 1600 Tysons Boulevard, McLean, VA 22102, US
SO Wila-IPA-2001-H52-T1
DT Patent
LA Application in English
DS W AE; W AG; W AL; W AM; W AT; W AU; W AZ; W BA; W BB; W BG; W BR; W BY; W BZ; W CA; W CH; W CN; W CO; W CR; W CU; W CZ; W DE; W DK; W DM; W DZ; W EC; W EE; W ES; W FI; W GB; W GD; W GE; W GH; W GM; W HR; W HU; W ID; W IL; W IN; W IS; W JP; W KE; W KG; W KP; W KR; W KZ; W LC; W LK; W LR; W LS; W LT; W LU; W LV; W MA; W MD; W MG; W MK; W MN; W MW; W MX; W MZ; W NO; W NZ; W PL; W PT; W RO; W RU; W SD; W SE; W SG; W SI; W SK; W SL; W TJ; W TM; W TR; W TT; W TZ; W UA; W UG; W US; W UZ; W VN; W YU; W ZA; W ZW;
RW AT; RW BE; RW CH; RW CY; RW DE; RW DK; RW ES; RW FI; RW FR; RW GB; RW GR; RW IE; RW IT; RW LU; RW MC; RW NL; RW PT; RW SE; RW TR; RW AM; RW AZ; RW BY; RW KG; RW KZ; RW MD; RW RU; RW TJ; RW TM; RW GH; RW GM; RW KE; RW LS; RW MW; RW MZ; RW SD; RW SL; RW SZ; RW TZ; RW UG; RW ZW; RW BF; RW BJ; RW CF; RW CG; RW CI; RW CM; RW GA; RW GN; RW GW; RW ML; RW MR; RW NE; RW SN; RW TD; RW TG
PIT WOA2 PCT-PUBLICATION
PI WO 2001097794 A2 20011227
OD 20011227
AI WO 2001-US18773 20010612
PRAI US 2000-213073 20000621

L13 ANSWER 5 OF 5 PATOSWO COPYRIGHT 2002 WILA
AN 2000:906967 PATOSWO ED 20000921 EW 200037 FS OS
TI **MATRIPTASE**, A SERINE PROTEASE AND ITS APPLICATIONS.
IN DICKSON, Robert, B., 10407 Barrie Avenue, Silver Spring, MD 20902, US;
LIN, Chen-Yong, 7610 Shreve Road, Falls Church, VA 22043, US;
JOHNSON, Michael, 12911 Margot Drive, Rockville, MD 20853, US;
WANG, Shaomeng, 1112 Regal Oak Drive, Rockville, MD 20852, US;
ENYEDY, Istvan, Apartment 302, 3216 Chillum Road, Mount Rainier, MD 20712, US
PA GEORGETOWN UNIVERSITY, 4000 Reservoir Road, N.W., Washington, DC 20007, US (except US);
DICKSON, Robert, B., 10407 Barrie Avenue, Silver Spring, MD 20902, US (only US);
LIN, Chen-Yong, 7610 Shreve Road, Falls Church, VA 22043, US (only US);
JOHNSON, Michael, 12911 Margot Drive, Rockville, MD 20853, US (only US);
WANG, Shaomeng, 1112 Regal Oak Drive, Rockville, MD 20852, US (only US);
ENYEDY, Istvan, Apartment 302, 3216 Chillum Road, Mount Rainier, MD 20712, US (only US
AG TESKIN, Robin, L. et al., Burns, Doane, Swecker & Mathis, LLP, 1731 King

Street, Suite 500, P.O. Box 1404, Alexandria, VA 22313-1404, US
SO Wila-IPA-2000-H37-T1
DT Patent
LA Application in English
DS W CA; W JP; W US;
RW AT; RW BE; RW CH; RW CY; RW DE; RW DK; RW ES; RW FI; RW FR; RW GB;
GR; RW IE; RW IT; RW LU; RW MC; RW NL; RW PT; RW SE
PIT WOA1 PCT-PUBLICATION
PI WO 2000053232 A1 20000914
OD 20000914
AI WO 2000-US6111 20000310
PRAI US 1999-124006 19990312

=>